



Dietary Cation-Anion Difference in Cattle: Implications for Health and Productivity

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INTRODUCTION

The transition period of farm animals usually involves 3 weeks prepartum to 3 weeks after calving. During this phase, the energy demands increase, owing to the growth of the fetus and also the development of the mammary gland. Consequently, it poses the system in pressure resulting in a Negative Energy Balance (NEB) (Martinez *et al.*, 2018; Trevisi and Minuti, 2018). Therefore, this phase encompasses the alteration of energy and mineral metabolism, disturbances in the hormone interaction, and reduced feed intake, which predisposes the animal to metabolic diseases like milk fever (hypocalcemia), ketosis, abdominal displacement, ruminal acidosis, and mastitis (Drackley *et al.*, 2005; Melendez and Risco, 2016).

Nutritional intervention may be a pivotal factor in reducing or alleviating metabolic diseases in farm animals. Dietary cation-anion difference (DCAD) is presently the crucial target in formulating the ration for post-partum or lactating animals. The dietary cation-anion difference (DCAD) is the difference, in millequivalents/100g DM (meq), between biologically strong cations (Na and K) and anions (Cl and S) in the diet (Bani Hassan *et al.*, 2018). Although other minerals have an impact on acidbase metabolism, the four minerals used in dietary cation-anion difference have the greatest effect. Manipulation of acidbase balance can be used to manipulate other biological functions to benefit health and productivity of cows.

ROLE OF DIETARY CATION-ANION BALANCE IN RUMINANTS

Mongin (1980) was among the first to suggest a complex relationship involving dietary sodium (Na), potassium (K), and chloride (Cl). Adjusting dietary anions (Cl-) against cations (Na+ and K+) is crucial for optimizing the physiological functions of animals. The levels of Na+, K+, and Cl- in the diet need to be adequate to maintain osmotic balance, acid-base equilibrium, and ruminants' indirect role in the Na+ and K+ cellular pumps, lactation performance, calcium metabolism in prepartum dairy cows, and phosphorus metabolism in young calves (Hynd, 2019; NASEM, 2021). Sodium and potassium are taken in from the gastrointestinal tract by releasing a proton, while chloride and sulfur are often absorbed by releasing a bicarbonate ion (Goff, 2018). These characteristics suggest that a high positive dietary cation-anion difference (DCAD), calculated as the mEq of Na + K – Cl – S per kilogram of dry matter, can help prevent metabolic acidosis. Increasing the DCAD from negative or neutral to strongly positive values boosts dry matter intake (DMI) and milk production (Hu *et al.*, 2007; Glosson *et al.*, 2020; Hassanien *et al.*, 2023; Bach *et al.*, 2023). Alongside performance gains, raising the DCAD boosts blood pH, blood bicarbonate concentration, and urine pH, indicating an impact on blood acid-base balance (Do Nguyen *et al.*, 2022; Hassanien *et al.*, 2022; Melendez *et al.*, 2022). A positive DCAD can also influence rumen fermentation and raise ruminal pH. Its ruminal buffering effect is complicated by the method of increasing DCAD through changes in sodium bicarbonate content, despite sodium bicarbonate being a well-known ruminal buffer (Feizdar Barabady *et al.*, 2023; Khani *et al.*, 2024).

Dietary cation-anion differences play a significant role in regulating blood acid-base levels primarily through adjustments in renal function. When animals are fed low DCAD diets, the renal mechanisms responsible for acid excretion and bicarbonate reabsorption may not adequately prevent a significant drop in blood bicarbonate levels and pH. Increasing the DCAD helps the animal's metabolism overcome the limitations of renal mechanisms in conserving bicarbonate, leading to an increase in blood bicarbonate concentration. This excess bicarbonate can be partially recycled into the rumen to counteract pH decreases and can also help neutralize excess protons at the metabolic level (Suman *et al.*, 2021; Zynda, 2021; Zhang *et al.*, 2022).

DCAD AND TRANSITION COW

Modifying the diet composition during the prepartum period can have enduring effects on the subsequent lactation. Generally, dry cows are provided with diets that fulfill the nutritional requirements of both the dam and offspring while avoiding excessive nutrient intake to limit body fat accumulation. Conversely, cows in the final three weeks of gestation are given diets that meet their nutritional needs while also being formulated to minimize the likelihood of peripartum metabolic disorders. One strategy involves adjusting the concentrations of strong ions in the diet to influence the prepartum dietary cation-anion difference (DCAD) (Vieira-Neto *et al.*, 2024).

Extensive evidence shows that feeding acidogenic diets before calving reduces the risk of milk fever during lactation initiation. This finding prompted the practice of feeding diets with a higher proportion of anions compared to cations to alleviate milk fever issues (Lean *et al.*, 2019; Santos *et al.*, 2019; Cariappa *et al.*,

2022). The elevated blood calcium levels not only prevented milk fever but also reduced instances of retained placenta and displaced abomasum, which were linked to calcium deficiency hindering muscle contractions (Nurye and Animut, 2022). Consequently, nutritionists began recommending prepartum diets for cows with fewer cations than anions to boost blood calcium levels around calving when deficiencies were most critical. These diets are known as anionic diets or diets with a low or negative cation-anion difference. Providing prepartum dry cows with reduced levels of sodium (Na) and potassium (K) compared to chloride (Cl) and sulfur (S) boosts blood calcium levels during calving. The formulation's negative dietary cation-anion difference (DCAD) induces a compensated metabolic acidosis in prepartum cows. Elevated levels of dietary anionic salts result in a systemic influx of negatively charged ions, causing a rise in hydrogen ion concentration to uphold electro-neutrality. This elevated hydrogen ion concentration triggers a mild metabolic acidosis. This condition lowers urine pH and increases calcium excretion in the urine (Berwal *et al.*, 2020; Hassanien *et al.*, 2022). Compensated metabolic acidosis also directly impacts calcium availability by promoting bone resorption and enhancing tissue responsiveness to hormonal cues. In the context of prepartum compensated metabolic acidosis, calcium is actively and passively absorbed from the rumen and small intestine. Additionally, it is mobilized from bone reserves and then excreted through urine to maintain balance. This continual calcium flux ensures a readily available supply of calcium for the onset of lactation, especially when urinary calcium excretion is conserved (Nurye and Animut, 2022; Vieira-Neto *et al.*, 2024)

It's crucial to note that in trials where negative dietary cation-anion difference (DCAD) helped prevent milk fever, the diets were characterized by elevated calcium concentrations, typically around 1.5% Ca.

Negative DCAD is associated with increased urinary calcium excretion. Therefore, if the dietary calcium levels were low while employing a negative DCAD, there is a risk of hypocalcemia, which can occur independently of and unrelated to milk fever. Conversely, achieving success with this approach may necessitate high dietary calcium levels combined with a low DCAD (Couto Serrenho, 2020).

While much of the focus on dietary cation-anion difference (DCAD) manipulation is on prepartum cows to prevent milk fever, it can also be relevant postpartum. Providing a highly positive DCAD diet during early lactation can be beneficial for maximizing milk yield and maintaining cow health (Mushfiq *et al.*, 2023). Potassium supplementation, is crucial for rumen health, enhanced productivity, and increased milk fat content, especially in closed intensive farming systems (Çınar and Şen, 2022; Elmhadi *et al.*, 2022). Certain feed sources, like quality pastures and handfed roughage, typically supply sufficient cations for a highly positive DCAD. Additionally, incorporating sodium bicarbonate to counter ruminal acidosis in cows on high-concentrate diets can be beneficial for boosting DCAD levels during the production phase (Zachwieja *et al.*, 2022)

ESTIMATION OF DIETARY CATION-ANION BALANCE

Assessing urine [Ca²⁺] offers valuable insights into calcium dynamics during the periparturient period in cows (Vagnoni and Oetzel, 1998). It seems that monitoring urine [Ca²⁺] could be the most effective way to gauge the risk of periparturient hypocalcemia and assess the efficacy of feeding a DCAD ration. For a comprehensive understanding of acid-base balance in healthy cattle, measuring urine net acid excretion (NAE) or net base excretion (NBE) is crucial. However, when urine pH falls within the range of 6.3 to 7.6, it

provides a cost-effective and clinically informative view of acid-base balance in cattle (Melendez *et al.*, 2021). This is because changes in urine pH within this range closely mirror changes in NAE or NBE. Higher urinary pH levels can indicate increased blood HCO₃ and reduced urine net acid excretion, suggesting a significant decrease in the acid load of lactating cows with higher DCAD intake (Hu *et al.*, 2007).

Urine seems to be the preferred fluid for monitoring calcium levels and acid-base status in dairy cattle (Constable *et al.*, 2019). While measuring urinary strong ion difference, NAE, or NBE is more resource-intensive and costly compared to urine pH measurement, it has been challenging to implement on farms. However, the general electroneutrality equation for urine indicates that in alkaline urine (especially when pH > 8.0), urine strong ion difference is approximately equal to urine [HCO₃⁻] because [NH₄⁺] is negligible, leading to NBE being approximately equal to [HCO₃⁻]. Consequently, analyzing total CO₂ using an automatic analyzer in an anaerobically collected and stored urine sample (ensuring no Pco₂ loss from urine) could offer a straightforward yet clinically valuable method for determining NBE in alkaline urine samples from cattle (Constable *et al.*, 2010; Berend and Duits, 2019; Reddi, 2020; Gärtner *et al.*, 2019).

Changes in dietary cation-anion difference (DCAD) had a significant quadratic impact on urine pH, with pH increasing as DCAD increased. This increase in urine pH was associated with higher blood bicarbonate (HCO₃) levels and a decrease in urine net acid excretion, indicating a substantial reduction in the acid load on lactating cows as DCAD increased. The excretion ratios of potassium (K) and chloride (Cl), measured as mg/L relative to creatinine concentration in urine, increased proportionally with their dietary concentrations. However, sodium (Na) excretion exhibited a quadratic change in

response to its dietary concentration. These variations mirrored slight shifts in blood mineral levels, particularly Na and K, resulting from the dietary intervention (Block, 2002).

DCAD FEEDING STRATEGY

Development of feeding strategies depends on the anion and cation concentrations in feed and the length of feeding interval. Feed ingredients with varying cation and anion concentrations are selected to formulate diets with the desired DCAD levels. High-cation feeds such as potassium sources (e.g., potassium carbonate, potassium bicarbonate) (Alfonso-Avila *et al.*, 2017) and low-anion feeds (e.g., grains, corn silage) can be used to increase DCAD, while high-anion feeds (e.g., ammonium chloride) can be used to decrease DCAD (Mueller *et al.*, 2001). Supplementing the diet with specific cations or anions, such as potassium or chloride salts, can be used to adjust DCAD levels in ration. This supplementation can be particularly important in situations where dietary sources do not provide sufficient cations or anions to achieve the desired DCAD balance (Valldecabres and Silva-del-Río, 2023). The sulphate salts are added to obtain maximum of 0.4 to 0.45% Mg and S in diet. The chloride salts are used to adjust the DCAD between -10 to -15 meq/100g dietary DM. Calcium intake should be raised to around 120 to 150 g per cow each day. The recommended DCAD range of -10 to -15 meq/100g of DM might indeed be lower than the actual requirement to maintain the acid-base balance and the calcium homeostasis in body (Block, 2002). However, this range offers a safety margin to accommodate for variations in potassium (K) concentrations in feeds and forages consumed by the animal. Management and maintenance of the DCAD within the recommended range optimizes calcium metabolism and minimize the risk of metabolic disorders related to acid-base imbalance (Zimpel, 2021; Caixeta and Omontese, 2021).

Regular monitoring of dietary DCAD levels is essential to ensure to align with the specific needs of the herd. DCAD levels may need to be adjusted based on factors such as stage of lactation, milk production level, environmental conditions, and individual cow responses.

DCAD AND HEALTH CHALLENGES

Dietary Cation-Anion Difference imbalance in cattle can lead to several health challenges, primarily the metabolic disorders and metabolism of the animals, particularly in dairy cows (Nikkhah *et al.*, 2023). Here are some health challenges associated with DCAD imbalance in cattle:

1. Metabolic Acidosis or Alkalosis:

DCAD influences the acid-base balance in the body. If the DCAD is too high (positive), it can lead to metabolic alkalosis, and if it's too low (negative), it can result in metabolic acidosis (Zhang *et al.*, 2022). Both conditions can have adverse effects on cow health and productivity (Vieira-Neto *et al.*, 2024).

2. Milk Fever: One of the most well-known consequences of imbalanced DCAD in dairy cows is the risk of milk fever (DeGaris and Lean, 2008). During the transition period, dairy cows experience a sudden increase in calcium demand for colostrum and milk production (Horst *et al.*, 1997). If dietary calcium intake is insufficient, or if calcium absorption and mobilization are compromised due to acidosis, cows may develop hypocalcemia, characterized by weakness, muscle tremors, recumbency, and impaired muscle function (McArt and Neves, 2020). A negative DCAD diet before calving helps to prevent milk fever by stimulating calcium mobilization from the bones to support milk production (Weich *et al.*, 2013). However, if the DCAD is too low, it can lead to excessive calcium mobilization, resulting in milk fever (Wuz *et al.*, 2014).

3. Suboptimal Production: Imbalances in DCAD can also lead to reduced feed intake, decreased milk yield, and impaired reproductive performance in dairy cows (Lopera *et al.*, 2018; Santos *et al.*, 2019). This is because DCAD affects rumen pH, which in turn influences nutrient utilization and overall cow health (Zimpel *et al.*, 2018).

4. Urolithiasis: In beef cattle, imbalances in DCAD can contribute to the formation of urinary calculi (stones) in the urinary tract (Jones *et al.*, 2009). High DCAD diets can increase the risk of urinary calculi formation due to elevated urinary pH, leading to potential blockages and urinary tract issues (Osborne *et al.*, 1985).

Monitoring urine pH and adjusting dietary electrolyte levels are common strategies to maintain proper DCAD balance and prevent associated health issues in cattle (Amanlou *et al.*, 2008).

DCAD AND PHYSIOLOGICAL CHALLENGES

Transition period is marked by various physiological challenges in cattle (Heron *et al.*, 2009). Here are some of the key physiological challenges associated with DCAD imbalance in cattle:

1. Acidosis: When the DCAD is too low (acidic diet), it can lead to metabolic acidosis in cattle (Zachwieja *et al.*, 2022). The excess of anions, such as chloride and sulfur, leads to increased acid production in the rumen during fermentation. This results in the accumulation of acidic byproducts, such as lactic acid and volatile fatty acids (VFAs), leading to a decrease in rumen pH (Nguyen *et al.*, 2020). The disturbances in rumen function and microbial population lead to reduced feed intake, diarrhoea, lameness, and a decrease in milk production (Yang *et al.*, 2021).

2. Alkalosis: Alkalosis occurs when the DCAD is high, indicating an excess of dietary cations (like potassium and sodium) relative to dietary anions (like chloride and sulfur) in body (Melendez *et al.*, 2022). This imbalance results in an alkaline environment in the rumen and body tissues (Hassanien *et al.*, 2023). The excess of cations, such as potassium and sodium, can lead to increased production of alkaline substances in the rumen (Hassanien *et al.*, 2022). The reduced rumen motility and decreased microbial activity leads to alterations in nutrient metabolism (Goff *et al.*, 2020). Alkalosis can cause electrolyte imbalances, leading to weakness, muscle twitching, and reduced milk production (Neves *et al.*, 2018). Alkalosis is less common than acidosis in cattle (Roussel *et al.*, 2014).

3. Calcium homeostasis: Calcium metabolism is vital for various physiological functions, including skeletal health, muscle contraction, nerve transmission, and milk production (Seifi and Kia, 2018). DCAD imbalance can disrupt calcium homeostasis, the balance between calcium intake, absorption, excretion, and mobilization from bone reserves (Wilkens *et al.*, 2019). Acidosis alters the pH in the gut, potentially reducing the solubility and availability of calcium for absorption. When calcium absorption is impaired and bone resorption is increased and the body may compensate it by increasing renal reabsorption of calcium from the urine (Horst *et al.*, 2021). Prolonged acidosis can overwhelm this compensatory mechanism leading to low blood calcium levels (Glosson *et al.*, 2020). Hypocalcemia predispose cows to conditions like milk fever (parturient paresis) and other metabolic disorders around calving (DeGaris and Lean, 2008).

Calcium metabolism is also crucial for reproductive health in cattle (Seely and McArt, 2023). It influences ovarian function, uterine health, and embryo development. DCAD imbalances causes irregular estrous cycles,

decrease fertility rates, and increase the risk of uterine infections and embryonic losses in dairy cows (Thakur *et al.*, 2022). A low DCAD diet can also stimulate bone resorption, where calcium is released from the bones into the bloodstream to help buffer the acidic conditions. Chronic acidosis can lead to increased osteoclastic activity (cells responsible for breaking down bone tissue), resulting in demineralization of bone matrix and weakening of skeletal structure. This process can predispose cattle to conditions like osteoporosis and osteomalacia, where bones become brittle and prone to fractures. Supplementing calcium sources during the post partum period can help mitigate the risk of hypocalcemia and its associated health issues in dairy cows (Bonjour, 2013).

4. Hormonal Imbalance: Hormonal regulation in cattle is affected by the anion cation balance in diet. Hormonal disturbances is primarily through its effects on the acid-base balance and metabolic processes in the body (Suman *et al.*, 2021). Acidosis resulting from a low DCAD diet can trigger the release of stress hormones such as cortisol (Shahzad *et al.*, 2007). Cortisol is released in response to stress and helps the body cope with adverse conditions. However, chronically elevated cortisol levels due to acidosis can have detrimental effects on overall health, including immune suppression, muscle breakdown, and decreased fertility (Fernandez-Novo *et al.*, 2020). Insulin Sensitivity is also influenced by DCAD imbalance in cattle. Acidosis disrupts normal carbohydrate metabolism, leading to insulin resistance in peripheral tissues, resulting in elevated blood glucose levels. Prolonged insulin resistance can contribute to metabolic disorders like laminitis and fatty liver syndrome (Vieira-Neto *et al.*, 2021).

Acidosis affects the normal secretion and function of reproductive hormones in cattle. It can interfere with the pulsatile release of gonadotropin-releasing hormone (GnRH) from

the hypothalamus, which is vital for the regulation of reproductive cycles. As a result, acidosis may lead to irregular estrous cycles, delayed ovulation, and decreased fertility in cow (Sammad *et al.*, 2022). Thyroid hormones play a key role in regulating metabolism, growth, and energy balance. Acidosis-induced stress can suppress thyroid function, leading to decreased production of thyroid hormones such as thyroxine (T4) resulting in metabolic slowdown, reduced feed efficiency, and impaired growth and reproduction (Żarczyńska, and Świerczyński *et al.*, 2023).

Chronic acidosis contribute to adrenal gland malfunction in cattle. The adrenal glands produce hormones such as aldosterone and adrenaline, which are involved in electrolyte balance, stress response, and blood pressure regulation (Gałęska *et al.*, 2022). Acidosis-induced stress can alter adrenal hormone secretion, leading to electrolyte imbalances and cardiovascular disturbances. Abnormal metabolic processes and nutrient utilization interfere with the GH release from the pituitary gland. Changes in GH levels can influence growth rates, body composition, and milk production in cattle (Leduc *et al.*, 2021).

5. Reproductive Issues: Reproductive issues are a significant concern in dairy cattle production, and DCAD imbalance can indeed contribute to various reproductive problems (Serrenho *et al.*, 2021). Cows may experience delayed onset of estrus or irregular estrus periods. This can lead to challenges in detecting estrus, which is essential for successful breeding and conception. Acidosis-induced metabolic disturbances causes reduced follicular development, ovulation rates, and conception rates (Venjakob *et al.*, 2017). Cows may have difficulty conceiving or may experience early embryonic death, resulting in prolonged calving intervals and reduced reproductive efficiency. Acidosis can adversely affect oocyte (egg) quality in dairy cows (Hammon *et al.*, 2000). Suboptimal conditions

in the reproductive tract due to acidosis can compromise the development and maturation of oocytes, leading to lower fertilization rates and decreased embryo quality (Pawlinski *et al.*, 2023). This can result in reduced pregnancy rates and increased embryonic losses in affected cows.

DCAD imbalance can also impact uterine health in dairy cattle (Ryan *et al.*, 2020). Acidosis-induced changes in uterine pH and microbial populations can increase the risk of uterine infections such as metritis and endometritis. These infections can impair fertility by disrupting normal uterine function and compromising embryo survival (Reinhardt *et al.*, 2011; Miltenburg *et al.*, 2016). Moreover, it increases the susceptibility of embryos to mortality during early development. Suboptimal uterine conditions and compromised oocyte quality can contribute to higher rates of embryo mortality, particularly during the critical early stages of pregnancy (Fares *et al.*, 2022). Acidosis, may predispose dairy cows to retention of fetal membranes (placenta) after calving. It impairs uterine contraction and clearance mechanisms, leading to delayed expulsion of fetal membranes (Janocha *et al.*, 2020). Retained fetal membranes can increase the risk of uterine infections and negatively impact fertility and reproductive performance. Implementing effective reproductive management practices, such as proper estrus detection, timely breeding, and proactive monitoring of uterine health, can help mitigate the impact of DCAD imbalance on reproductive outcomes in dairy herds.

6. Heat Stress Susceptibility: Acidosis can increase the susceptibility of cattle to heat stress (Burhans *et al.*, 2022.) impairing normal thermoregulation mechanisms. Sodium and potassium are essential for maintaining hydration, nerve function, and muscle contraction. During heat stress, cattle lose electrolytes through sweating and panting to

regulate body temperature (ElShwey *et al.*, 2017). Cattle may reduce feed intake due to decreased appetite (Becker *et al.*, 2020) and metabolic changes aimed at dissipating excess body heat. Reduced feed intake leads to the negative energy balance experienced by cattle during heat stress, leading to further metabolic challenges and decreased resilience to heat stress. Increased DCAD improves rumen function, nutrient absorption (Martins *et al.*, 2016) and metabolic efficiency, making cattle less susceptible to the negative effects of heat stress. Proper DCAD balance is essential for maintaining optimal physiological function and heat tolerance in cattle. An appropriate DCAD balance supports electrolyte balance, acid-base homeostasis (Wildman *et al.*, 2007), and metabolic efficiency, which are critical for coping with heat stress. Imbalanced DCAD can compromise these mechanisms, reducing the ability of cattle to regulate body temperature and withstand heat stress (Suman *et al.*, 2021). Proper management of DCAD balance through dietary formulation is essential for supporting cattle health and resilience to heat stress (Bertens *et al.*, 2023), particularly in environments prone to high temperatures.

CONCLUSION

Managing DCAD balance through proper dietary formulation is essential to prevent these physiological challenges and maintain the overall health and productivity of cattle. This often involves adjusting the levels of dietary cations and anions to ensure they meet the specific nutritional requirements of the animals at different stages of production to achieve an appropriate balance of dietary cations and anions to support metabolic health and minimize the risk of acidosis.

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